A 21-year-old Woman who had a Complicated Birth

Katherine Fichtel; and Mamta Modhwadia, MD

The patient was a 21-year-old woman who had a complicated birth. When she was born, she had aspirated meconium, had apnea, and had an 8-day stay in the neonatal intensive care unit (NICU).

At the time of her admission, the woman lived with her parents and her 18-year-old sister in a home located in the same town where she graduated from high school with academic success. At admission, she was entering her senior year at a local college, where she had previously made the dean’s list.

She denied a history of substance or alcohol use and was noted by her family to be a “rule follower” who had trouble “fitting in.” Her parents described her as shy and polite with strangers and acquaintances, but they said she was stubborn at home. Over the past few years, her parents said she preferred to spend much of her free time alone on the Internet or doing schoolwork.

The patient had a self-reported history of depression since she was 13 years old, but she denied past psychiatric hospitalization or treatment. When she was 17 years old, she twice impulsively expressed suicidal ideation to her parents, but her parents said she quickly retracted these statements. She reported a history of visual hallucinations, consisting of bugs, for “as long as I can remember.”

Two years before her psychotic episode and hospitalization, an EEG showed mild diffuse slowing. Magnetic resonance imaging (MRI) of the brain showed right parieto-temporal and periventricular encephalomalacia. The patient’s family history was significant for bipolar disorder in her mother, who was recently diagnosed, and her maternal aunt.

According to the family, the patient had demonstrated increased frustration and sadness in the month leading up to her admission. In one instance, she returned home extremely agitated after attending a barbecue with friends, declaring that “no one understands me.” The patient often was observed staring at her computer, completely unaware of her surroundings for minutes at a time, then suddenly becoming attentive again without an understanding of time having passed. She experienced insomnia but denied decreased appetite or weight loss.

This was the patient’s first psychiatric hospitalization. On the day of her arrival, the patient displayed a high level of anxiety and disorganized thinking. She felt her parents were imposters who were role-playing and were conducting a “social experiment” with her by “pretending to be my parents having a meeting.” She displayed no motor or neurologic deficits, and blood work was within normal limits.

A neurology consultation was requested to rule out encephalopathy, given the patient’s history of birth complications. Computerized tomography (CT) of the head was performed without contrast and demonstrated no acute changes. However, the scan confirmed a focal calcification in the right corona radiate with subjacent ex vacuo dilatation of the right lateral ventricle,
which may have been related to a previous hemorrhage or infarction.

During her hospital course, the patient was observed responding to internal stimuli, laughing to herself, and startling with a visual hallucination of seeing a “beetle.” Her mood fluctuated from distracted to anxious. Her speech had poor prosody, and her affect was flat, exhibiting response latency and thought-blocking.

She demonstrated paranoia regarding the safety of the drinking water, refusing to drink without reassurance, and expressed suspicion of the medications. Her attention was limited and short-term memory appeared impaired, as she could not recall team members’ positions and names.

Risperidone 2 mg twice daily and divalproex extended release 500 mg once daily significantly improved her target symptoms, decreasing mood lability, psychomotor agitation, visual hallucinations, and paranoia.

**DISCUSSION**

Psychotic disorders have been associated with developmental problems, including those related to obstetric complications. However, the connection between neuro-pathology and the psychotic phenotype of schizophrenia in the context of obstetrical complications is far from clarified. Neurodevelopmental models link fetal hypoxia with alterations in hormonal and serotonergic functioning, as well as anxiety-like behaviors.

Birth trauma, specifically ischemic events, has been correlated with reductions in frontal and temporal gray matter and cerebrospinal fluid volume in those at genetic risk for schizophrenia. In nonfamilial schizophrenia, obstetrical complications may be an environmental factor contributing to its development and are associated with lateral ventricular enlargement.

The patient’s presentation was consistent with first-onset psychosis that could represent the initial phase of a psychotic disorder, such as schizophreniform disorder or acute psychotic disorder, or bipolar disorder, given her family history. However, her history did not meet the 6-month duration criteria for schizophrenia or schizoaffective disorder.

A number of details about the patient’s history and presentation were unique. These included: 1) the patient’s history of having a difficult birth and an 8-day NICU stay; 2) significant brain MRI and head CT demonstrating right parieto-temporal and periventricular encephalomalacia, and lateral ventricular enlargement and atrophy, respectively; and 3) a familial predisposition to bipolar disorder.

Although many theories exist regarding the origin of schizophrenia, evidence points to the neurodevelopmental model in which developmental injuries in the late-first or early-second trimester lead to activation of pathologic neural circuits during adolescence or young adulthood, triggering the appearance of positive or negative symptoms. Individuals at risk for schizophrenia and those with a first episode of the disease are more likely to have a history of obstetric complications compared with normal subjects.

An approximately twofold increased risk for schizophrenia has been noted in all types of birth complication, specifically hypoxic events correlated to decreases in frontal and temporal gray matter and CSF volume in those at genetic risk for schizophrenia. Prenatal influenza infection, poor maternal nutrition, and prenatal stress may double the relative risk of the development of schizophrenia.

Other predisposing events, in all of which hypoxia may play a role, include cesarean delivery, pre- or postterm delivery, resuscitation, nuchal cord, breech position, low birth weight, use of high forceps, preeclampsia, premature rupture of membranes, multiple gestation, or abnormal labor duration. In humans, acute hypoxia of the fetus related to stress during pregnancy leads to a decline in gestational neuroactive steroid concentrations, normally maintained by the placenta, which are needed to protect the fetal brain from excitotoxic cell death and allow for cell proliferation.
Animal studies also support a neurodevelopmental explanatory model connecting fetal asphyxia with neural and behavioral dysfunction in offspring. One study showed that gestational hypoxia has the potential to enhance the activity of the hypothalamic-pituitary-adrenal axis and induce anxiety-like behavior in adult rat offspring. The disordered function of the HPA axis is related to the activation of the CRH-CRH1-NE neural circuit in these rats by enhanced expression of corticotropin-releasing hormone and its receptor (CRHR1) in the paraventricular nucleus and increased levels of norepinephrine and dopamine in the locus ceruleus.

It has, therefore, been concluded that stress during pregnancy might be a risk factor for impaired physiologic stress response and the development of anxiogenic behavior in offspring. The colocalization of CRH and its receptors and the CRH-NE stress system in the brain has been suggested as a possible neural basis of this behavioral change. Another study demonstrated that insults caused by fetal asphyxiation at critical periods of brain development led to a decrease in dorsal raphe serotonergic neurons and increased anxiety-related behavior, implying that fetal asphyxia may be associated with the development of affective disorders.

By defining the type and severity of obstetric complications in patients who later develop psychotic illness, it may be possible to identify dominant injuries that constitute vulnerability markers. Such findings could reveal the timing and nature of insults that may have subtle effects on the development and maturation of brain functions.

In addition, individuals with birth complications and their families may be vigilant for prodromal signs. Research focusing on these associations could assist in the creation of an instrument, similar to cardiovascular risk factor calculators used to predict risk of cardiovascular disease, which could more accurately estimate risk for psychotic illness.

CONCLUSIONS
A better understanding of the incidence and risk of perinatal complications and neurologic dysfunction in patients who later develop psychosis may better elucidate the pathologic etiology of psychotic disorders and allow for anticipation of prodromal signs. This report emphasized a case of a young woman whose first-onset psychosis may have origins in genetic and environmental stressors; in particular, a family history of bipolar disorder and a personal history of birth complications.

REFERENCES